Gastroesophageal Reflux Disease (GERD)

Objectives
- Have working knowledge of the anatomy and physiological mechanisms that contribute to GERD
- Gain knowledge to develop a consistent format for identifying GERD risk factors
- Know the epidemiology of GERD as it relates to patients lifestyle and healthcare delivery
- Know the atypical symptoms associated with GERD
- Know the alarm symptoms associated with GERD
- Know the treatment modalities for GERD and H-Pylori
- Know the relevant laboratory testing guidelines for the diagnosis and treatment of GERD and H-Pylori
- Know indications for referral and invasive evaluation of GERD
- Know the lifestyle modification issues for reducing GERD symptoms

GERD


GERD – Gallup Poll 2000
Most common complaints among U.S. adults (18 y.o or older)

65% Heartburn – Daytime and Nocturnal
62% Gas
55% Burning Sensation in Chest
52% Burning Sensation in Throat
50% Acid Reflux

GERD or GORD
- A description of a symptomatic condition or pathological alteration resulting from repeated episodes of gastric reflux.
- A digestive disorder affecting the LES.
- Multiple symptoms with esophageal and extraesophageal manifestations.

GERD or GORD

GERD
Difficult to obtain accurate epidemiological information due to the lack of standardized definition and diagnostic gold-standard.

Most epidemiological statistics assume Heartburn = GERD

Spechler SJ. Epidemiology and natural history of gastro-oesophageal reflux disease. Digestion 1992;51 suppl:24-9
### Difficult to obtain exact figures

- **1993**: "100 million adults suffer from heartburn"
- **1995**: "17–40 million adults"
- **2001**: "60 million adults"

25–40% experience GERD
7–10% daily


### Increasing global presence of GERD

18%–28% in North America

**El-Serag H. Update on the epidemiology of gastro-esophageal reflux disease; a systematic review. Gut doi:10.1136/gutjnl-2012-304269**

### ETHNICITY

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Prevalence Rate (per 100,000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>White population</td>
<td>556</td>
</tr>
<tr>
<td>African-Americans</td>
<td>288</td>
</tr>
<tr>
<td>Hispanics</td>
<td>48</td>
</tr>
</tbody>
</table>


### AGE and GENDER

- 74% of all GERD cases occur in women
- Other studies have noted prevalence but higher amounts of esophagitis in Men (2:1) and Barrets in Men (10:1)*
- >90% of GERD sufferers >25 y.o.


### GERD Diagnosis

216 percent increase

- **1998**: 995,402
- **2005**: 3,141,965


- 122% rise in Yearly hospitalizations with obesity diagnoses 1996-2004
- Casual association with obesity and gerd

At least one atypical symptom was present in patients with typical symptoms.


GERD – Symptoms

ATYPICAL
- Chest Pain
- Dysphagia
- Dyspepsia
- Asthma
- Voice change
- Globus
- Bronchitis
- Pneumonia

GERD – Symptoms

TYPICAL
- Heartburn
- Acid Regurgitation

Alarm Symptoms

- Dysphagia
- Odynophagia
- Early Satiety
- Weight loss
- GI blood loss
- Anemia
- New age >45
- Non-cardiac "angina-like" chest pain
- Failure of 4 wk acid suppression trial
- Breakthrough sxs

Asymptomatic

1993 study pH monitoring
- Reported in Hospital Physician August 1999 Estimated 30% of patients with GERD have no symptoms.
GERD –COSTS

DIRECT - 9.6 Billion dollars (Year 2000)

INDIRECT - consumption of health care and the lost days of work

479 Million dollars (Year 1998)


“PLOP-PLOP
FIZZ-FIZZ
OH WHAT A RELIEF
IT IS”

Direct Cost of Gastroesophageal Reflux Disorder (in millions)

Office Visits, $603.10
Hospital OPD, $212.90
Hospital ER, $77.50
Hospital Inpatient, $2,539.50
Drugs, $4,892.20


Affects of Heartburn on Quality of Life

GERD –Direct COSTS

GERD -Diagnosis

Clinical Diagnosis vs Dyspepsia

“Tests” are not necessary in patients with typical reflux symptoms

Trial of Therapy


Gallup 2000
Diagnosis

No gold standard exists for the diagnosis of GERD

Endoscopy - appropriate first-line investigation
? Once in lifetime with chronic symptoms (No ALARM)

24-hour pH monitoring reserved for atypical symptoms or fail to respond to proton pump inhibitor therapy.

GERD – Contributing Factors

Dietary and lifestyle choices: certain foods, smoking, obesity

Pregnancy - Most common condition predisposing to GERD 50 – 80% of pregnant patients report heartburn*.

Genetics plays a role; a recent study indicates that a family member of someone with GERD is four times more likely to experience the disorder

Meds


Myths

- Occ reflux isn’t bad
- Mint, milk will help soothe the sx
  - + licorice (anise helps)
- Avoid coffee, wine, juice, chocolate
- Avoid spicy foods

Fact

- There is no evidence to show that any of the dietary restrictions usually recommended make a difference.
- Evidence of a clear benefit from 2 lifestyle changes
  - Weight loss
  - Raising the head of your bed

Treatment

- Head of bed – laryngeal sx, cough, throat clearing, pharyngitis avoid recumbancy
- Small meals
- Food restrictions

STEP-UP

Proton pump inhibitor therapy

No relief with H2 at 2 weeks

Lifestyle modification + 8 week trial
  - b.i.d. H2 RA

Good response with H2 move to on-demand therapy
STEP-DOWN

Proton pump inhibitor therapy x 6-8 weeks

H$_2$ receptor antagonist or stop therapy

Step-down therapy has the merits of faster symptom relief, faster healing and overall costs less.

GERD

1998 Mortality Rate
0.48 deaths /100,000
-Centers for Disease Control


GERD – High Risk Patient

Patient with Alarm symptom

Age of onset
> 45 y.o. (> white males)

Significant ETOH of Tobacco use

Duration of symptoms
weekly heartburn sx > 5 years = 20-fold increased risk of adenocarcinoma of the distal esophagus or gastric cardia compared to non-heartburn patients.(NEJM)

GERD - Esophagitis

- Esophagitis – The squamous epithelium becomes altered secondary to excessive exposure of gastric juice from reflux.
- Low Grade – seen histopathologically
- High Grade – seen endoscopically

- Less than half of all GERD patients have EE


Endoscopy Screen

- GERD symptoms that are persistent or progressive despite appropriate medical therapy
- Dysphagia or odynophagia
- Involuntary weight loss > 5%
- Evidence of GI bleeding or anemia
- Finding of a mass, stricture, or ulcer on imaging studies
- Evaluation of patients with suspected extra-esophageal manifestations of GERD
- Screening for BE in selected patients (as clinically indicated - if negative no further screening)
- Persistent vomiting
- Evaluation of patients with recurrent symptoms after endoscopic or surgical antireflux procedures

GERD – Barrett Metaplasia

- Severe outcome of chronic GERD
  - Metaplastic columnar cells replace native squamous epithelium.

- Prevalence rate of less than 20% in the GERD patient population with African Americans having a higher rate than caucasians.*

- Patients at highest risk for Barrett's are Caucasian males with long duration (>5yrs) of reflux symptoms.

**Endoscopy Surveillance**

The cost effectiveness for patients without dysplasia is controversial. Appropriate for patients fit to undergo therapy.

Barret’s - Initial 2 screenings within one year.

- No dysplasia, after 2 consecutive examinations
- LGD
  - No specific protocol - annual. Fumar and bi 6 mo. from dx. If continued dysplasia consider yearly 6 mo.
- HGD
  - O times 1 year with multiple large capacity bx obtained at 6 mo intervals
  - If hist after 1 year dx CA the interval may lengthen if the dysplastic changes are noted on 2 subsequent endoscopies performed at 3-month intervals.

American Society for GI Endoscopy. ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. Gastrointestinal Endoscopy Journal Volume 63, No. 4 : 2006

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**ROME III**

The Rome criteria is a system developed to classify the functional gastrointestinal disorders (FGIDs), disorders of the digestive system in which symptoms cannot be explained by the presence of structural or tissue abnormality, based on clinical symptoms.


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**My Tummy Hurts**

**FUNCTIONAL HEARTBURN**

- Burning retrosternal discomfort
- Absence of evidence that gastroesophageal acid reflux is the cause of the symptom
- Absence of histopathology-based esophageal motility disorders

**FUNCTIONAL DYSPESPIA**

- Bothersome postprandial fullness
- Early satiation
- Epigastric pain/burning
- No evidence of structural disease (including at upper endoscopy)

3 mo sx onset 6 months prior to dx

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**H-Pylori**

GERD may worsen or develop for the first time after H pylori eradication.

- No effect on EGJ
- No effect on LES
- Unlikely effects esoph peristalsis or acid clearance

- Increases Gastrin levels but decreased acid secretion - cytokines inflammation
**H-Pylori Epidemiology**
- 20% < age 40
- 50% > age 60
- Uncommon in young children.
- > Low socio-economic status
- Immigration is responsible for isolated areas of high prevalence in some Western countries.
- Lowering rates

**H-Pylori**
- No effect on EGJ
- No effect on LES
- Unlikely effects on esoph peristalsis or acid clearance
- Increases Gastrin levels but decreased acid secretion – cytokines inflammation

**H-Pylori and Cancer**
- ~6 fold risk of gastric cancer
- Mucosa associated lymphoid tissue (MALT)
  - ~90% are associated with H. pylori.
  - ~50% cure for localized MALT after cure of H. pylori.

**Eurogast Study Group**

**H-Pylori Eradication**
- Increased risk of GERD
- Increased severity of esophagitis
- Lower prevalence of barrets and esoph adeno – gene dependent

**None of the above applicable in PUD**

**To Treat or not to Treat**
- H Pylori = 10 percent lifetime risk of developing peptic ulcer disease and 2-3 times increase of gastric adenocarcinoma.
  - Corpus dominant or Pan gastritis mild worsen GERD sx
  - Antral-dominant gastritis improvement of GERD sx
- H Pylori and GERD
  - H. pylori improves the ability of proton pump inhibitors (PPIs) to suppress acid.
- Chronic NSAID user
  - >12’s more likely to develop ulcer with H-Pylori presence

**Must Treat**
- Standard of care is to treat and test to cure:
  - Relatives of persons with gastric cancer
  - Patients in whom intestinal metaplasia has been detected on gastric biopsy
  - Infected spouses of patients who have been reinfected with H.pylori a second or third time after initial antibiotic treatment.
- H Pylori and PUD
  - 60 to 100 percent annual ulcer recurrence rate compared to 10 percent after eradication.
  - >85% Duodenal ulcers CagA strain
Tests
- PY-Test
  - Carbon 13 or 14 Urea Breath Tests
- Antibody testing
  - IgM - useless
  - IgG - best (+ up to 1 yr. negative could be too early assess with either treatment or length of sxs)
- Stool Antigen
- Endoscopy with biopsy

H-Pylori Meds
- Antibiotics
  - Amoxicillin, Clarithromycin, Metronidazole, Tetracycline
- H2-Blockers
  - Cimetidine (Tagamet), Famotidine (Pepcid), Nizatidine (Axid), Ranitidine (Zantac)
- Proton Pump Inhibitors (PPIs)
  - Esomeprazole (Nexium), Lansoprazole (Prevacid), Omeprazole (Prilosec), Pantoprazole (Protonix), Rabeprazole (Aciphex)
- Cytoprotective Agents
  - Bismuth subsalicylate, bismuth subcitrate potassium, sucralfate
- Combination Products
  - Helidac, Prevacid, Pylera

H-Pylori Treatment Regimens

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Single Drug Therapy</th>
<th>Two Drug Therapy</th>
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</thead>
<tbody>
<tr>
<td><strong>First Drug Regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Helidac + PPI</td>
<td>Low-Medium</td>
<td>84-94%</td>
</tr>
<tr>
<td>Lansoprazole + PPI</td>
<td>Low-Medium</td>
<td>84-94%</td>
</tr>
<tr>
<td>Pylera + PPI</td>
<td>Low-Medium</td>
<td>84-94%</td>
</tr>
<tr>
<td><strong>Three-Drug Regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bismuth + Metronidazole + Clarithromycin + PPI</td>
<td>Medium-High</td>
<td>greater than 80-90%</td>
</tr>
<tr>
<td>Bismuth + Amoxicillin + PPI</td>
<td>Medium-High</td>
<td>greater than 70-90%</td>
</tr>
<tr>
<td>Bismuth + Tetracycline + H2 Blocker</td>
<td>Medium-Medium</td>
<td>84-94%</td>
</tr>
<tr>
<td><strong>Two-Drug Regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin + Metronidazole</td>
<td>Medium-High</td>
<td>84-94%</td>
</tr>
<tr>
<td>Clarithromycin + Metronidazole</td>
<td>Medium-High</td>
<td>84-94%</td>
</tr>
<tr>
<td>Tindazole + PPI</td>
<td>Low-Medium</td>
<td>84-94%</td>
</tr>
</tbody>
</table>

Sequential Treatment
- 10 day treatment
  - PPI bid and Amox 1gm bid x 5 days
- Then -
  - Clarithromycin 500mg bid
  - Tindazole 500mg bid

CDC treatment
Omeprazole 40 mg QD + clarithromycin 500 mg BID x 2 wks, then omeprazole 20 mg QD x 2 wks
Ranitidine bismuth citrate (RBC) 400 mg BID + clarithromycin 500 mg TID x 2 wks, then RBC 400 mg BID x 2 wks
Bismuth subsalicylate (Pepto Bismol®) 525 mg QID + metronidazole 250 mg QID + tetracycline 500 mg QID x 2 wks + H2 receptor antagonist therapy as directed x 4 wks
Lansoprazole 30 mg BID + amoxicillin 1 g BID + clarithromycin 500 mg TID x 10 days
Lansoprazole 30 mg TID + amoxicillin 1 g TID x 2wks**
Ranitidine bismuth citrate 400 mg BID +clarithromycin 500 mg BID x 2 wks, then RBC 400 mg BID x 2 wks
Omeprazole 20 mg BID + clarithromycin 500 mg BID + amoxicillin 1 g BID x 10 days
Lansoprazole 30 mg BID + clarithromycin 500 mg BID + amoxicillin 1 g BID x 10 days

Potential proton pump inhibitors
- Safety concern

<table>
<thead>
<tr>
<th>PMI studied</th>
<th>Duration of studies</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastric carcinoids</td>
<td>Omeprazole, lansoprazole, pantoprazole</td>
<td>1-8 years</td>
</tr>
<tr>
<td>Gastric metaplasia/adenocarcinoma</td>
<td>Omeprazole</td>
<td>1-5 years</td>
</tr>
<tr>
<td>Gastric infections</td>
<td>Omeprazole</td>
<td>1 year</td>
</tr>
<tr>
<td>Mineral malabsorption</td>
<td>Omeprazole</td>
<td>6 months-2 years</td>
</tr>
<tr>
<td>B12 malabsorption</td>
<td>Omeprazole</td>
<td>10 years</td>
</tr>
</tbody>
</table>

PPI’s and Hips

- 10,834 hip fractures among nonusers of acid suppression agents and 2,722 hip fractures among PPI users.
- Patients using PPIs for longer than one year were estimated to have a hip fracture rate of 4.0 per 1,000 person-years compared with 1.8 per 1,000 person-years in acid suppression nonusers.
- Higher doses and longer use of PPIs were associated with higher fracture risk. The association also was stronger in men than in women.


Summary

- Difficult to obtain accurate epidemiological information due to the lack of standardized definition and diagnostic gold-standard.
- More prevalent in Whites
- Studies suggest may be more Prevalent in Women
- More prevalent in adults over 25

Summary

- May present with multiple symptoms, however Heartburn and Acid regurgitation considered most prevalent and synonymous with GERD.
- 50% state nighttime symptoms affect them more than daytime symptoms

Summary

- One of the top five prevalent and costly conditions affecting adults.
- 9.6 Billion Dollars in Direct Costs
- 5.9 billion dollars spent on GERD medications.
- Low Mortality Rate
- Significant disruption in life activities